Pediarix

We would like to begin this program with a discussion of a new pediatric combination vaccine. Combination vaccines are popular with clinicians and parents for the obvious reason- combination vaccines reduce the number of injections needed to complete the childhood immunization schedule.

In December 2002, the US Food and Drug Administration approved America's first pentavalent, or 5 component combination vaccine- Pediarix. This vaccine contains DTaP, hepatitis B, and inactivated polio vaccines. The DTaP component is Infanrix, and the hepatitis B component is Engerix-B.

The efficacy of Pediarix was not directly tested in clinical trials. Pediarix was approved by FDA based on the results of serologic testing for antibodies against the respective antigens, compared to children who received separate injections of DTaP, IPV, and hepatitis B vaccines. The level of antibody that is considered to be protective is reasonably well established for tetanus, diphtheria, polio and hepatitis B. The protective level of antibody for pertussis is less well established.

In the prelicensure studies, the proportion of children who developed a protective level of antibody, and the titer of antibody, was at least as high for the vaccine antigens given together as Pediarix as among children who received separate vaccines.

The minimum age for the first dose of Pediarix is 6 weeks, so it can not be used for the birth dose of the hepatitis B series. Pediarix is approved for the first three doses of the DTAP and IPV series, which are usually given at about 2, 4, and 6 months of age. However, Pediarix is approved for use through 6 years of age, the same as the DTaP component. This means that a child who is behind schedule can still receive Pediarix as long as it is given for doses one, two, or three of the series, and the child is less than 7 years of age. Pediarix is not approved for fourth or fifth doses of the DTAP series.

We have received numerous inquiries about doses of Pediarix inadvertently administered as booster doses. For instance, if Pediarix administered as a child's fourth or fifth dose of DTaP can be counted as a valid dose. I'll repeat here that FDA has not approved Pediarix for booster doses, so you should not use it in this situation. However, if Pediarix has been inadvertently administered as the fourth or fifth dose of DTAP or the fourth dose of IPV, it is not necessary to repeat the dose.

An important fact to remember about Pediarix, and for any other combination vaccine for that matter, is that the minimum intervals between doses are determined by the individual component with the longest minimum interval.

As a result, Pediarix minimum intervals are determined by the hepatitis B component. As for hepatitis B vaccine, the minimum interval between the first two doses of Pediarix is 4 weeks. The third dose should be administered at least 8 weeks after the second dose, and should follow the first dose by at least 16 weeks. The third dose is recommended at 6 months of age.

In 2002, the Advisory Committee on Immunization Practices, and the American Academy of Pediatrics stated a preference for administration of the first dose of hepatitis B vaccine shortly after birth, before the child leaves the hospital. This is an extremely important intervention to prevent transmission of hepatitis B virus to infants from undetected infected women.

A birth dose of hepatitis B vaccine does NOT prevent the routine use of a combination vaccine that contains hepatitis B vaccine - Pediarix or Comvax- beginning at 2 months of age. Either vaccine may be used if the infant receives a birth dose. In this situation, the infant will receive 4 doses of hepatitis B vaccine, but ACIP and AAP believe 4 doses of hepatitis B vaccine is an acceptable option if the provider chooses to use a combination vaccine that contains hepatitis B vaccine.

Engerix-B, the hepatitis B vaccine in Pediarix, has been shown to be effective in the prevention of perinatal hepatitis B virus transmission. However, GlaxoSmithKline did not provide data to the Food and Drug Administration for the use of Pediarix among infants born to women who were hepatitis B surface antigen positive, or whose surface antigen status was unknown.

Since the company did not provide supporting data, FDA did not approve Pediarix for this indication. Pediarix is approved by FDA only for use in infants born to women who are hepatitis B surface antigen negative. It is not approved for infants of HBsAg positive women, or women whose HBsAg status is not known. This could be a major impediment to the use of Pediarix, since in immunization practice you often do not know the mother’s hepatitis B surface antigen status.

In the prelicensure trials, it was observed that 100 percent of children who received three doses of Pediarix developed a protective level of anti-HBs antibody – that is 10 milli-international units per milliliter or higher. The average titer of anti-HBs antibody in Pediarix recipients was 16 hundred milli-international units per milliliter, compared to an average of 800 units per milliliter for children who received single antigen hepatitis B vaccine. This does NOT mean that Pediarix is twice as good as single antigen vaccine. What it DOES mean is that

the response to hepatitis B vaccine given as Pediarix is not inferior to the response when single antigen hepatitis B vaccine is given separately.

The Advisory Committee on Immunization Practices discussed this issue at length at it's February 2003 meeting. In the Committee's opinion, there is no evidence that infants of HBsAg positive women would respond to the hepatitis B component any differently than infants of HBsAg negative women.

As a result, ACIP approved the use of Pediarix among infants whose mothers are HBsAg positive, or whose surface antigen status is not known, even though FDA has not approved it for this use. ACIP made a similar recommendation for the use of Comvax several years ago. This recommendation was published in the 2003 hepatitis B Vaccines For Children resolution, which is available on the National Immunization Program website. We will provide a link to this document on our broadcast resources web page.

The safety of Pediarix was studied in prelicensure trials. The rates of a variety of local and systemic adverse reactions were compared in children who received Pediarix and those who received the component vaccines individually. There was no significant difference in local reactions, such as redness or swelling among the two groups. A larger proportion of children who received Pediarix reported a fever within 4 days of administration than those who received separate injections. Fever of 100.4 Fahrenheit occurred in 28 percent of Pediarix recipients compared to 20 percent who received separate vaccines. There was no difference in other systemic reactions, such as crying, restlessness, or loss of appetite.

Contraindications and precautions to a combination vaccine are the same as those for all the individual components, in this case DTaP, IPV, and hepatitis B vaccine. Most contraindications are driven by the pertussis component.

CDC has established a contract for Pediarix with the manufacturer. As I mentioned earlier, Pediarix has been added to the hepatitis B, IPV, and DTaP VFC statements. The decision to make Pediarix available through the Vaccine For Children program will be decided by individual states. You should check with the state VFC coordinator for the availability of Pediarix in your area.